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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/085,853	10/18/2001	Bertrand Merot	14138.1USD1	3281

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EXAMINER	
WAX, ROBERT A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/085,853	MEROT ET AL.	
	Examiner	Art Unit	
	Robert A. Wax	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities: the term "pyrole" is misspelled. It should read "pyrrole". This objection applies to claim 44 as well.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 43-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 43, 44 and 50-52 read on a hemin protein wherein the protein of animal origin is literally any protein of animal origin. Claims 45-49 specify the protein to be a "variant" of α- and/or β-globin. The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art.

The criteria for determining undue experimentation, summarized in *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988), are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in that art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404).

As stated above, claims 43, 44 and 50-52 read on a hemin protein wherein the protein of animal origin is literally any protein of animal origin. In the instant case 1) the quantity of experimentation would be enormous since there is an extremely large number of proteins to test, 2) the direction provided by the specification is limited to α- and/or β-globin, 3) the specification contains no teaching of any animal protein other than a globin that could be combined with a porphyrin group of plant origin and reversibly bind oxygen, 4) the nature of the invention is a combination of a plant oxygen-binding group with an animal protein, 5) the prior art contains no such teaching except

applicants' own art, 6) the level of skill in this art is very high, 7) the predictability is low for proteins other than α- and/or β-globin since it is unclear which structural features of a protein confer oxygen binding properties and 8) the claims include literally any protein of animal origin, thus the breadth is enormous.

Thus, when all the Wands factors are considered together, the conclusion that the practice of the claimed invention would require undue experimentation is inescapable.

Again, as stated above, claims 45-49 specify the protein to be a "variant" of α- and/or β-globin. The specification defines “variants” of α- and/or β-globins to include "one or more amino acid substitution(s), deletion(s) or insertion(s)" (page 7, lines 7-8) and that it "exhibits at least 90%, and preferably at least 95% homology or identity with the natural sequence" (page 7, lines 9-11). Further definitions include fragments of polypeptide chains or longer sequences (page 7, third paragraph).

Analysis of the Wands factors shows the following. 1) the quantity of experimentation necessary is huge since the number of possible mutations is immense, 2) the amount of direction or guidance presented is essentially zero; the specification provides inadequate guidance to allow the skilled artisan to determine which of the myriad possible substitution, deletion and insertion mutants of α- and/or β-globins would be likely to reversibly bind oxygen when combined with a porphyrin nucleus, nor does the specification provide guidance regarding, for example, the domain structure of the protein, the location of the site which confers oxygen binding capability, or sites of interaction with other proteins, cofactors or regulatory molecules. In order to predict with

reasonable assurance the effect that different substitution, deletion and/or insertion mutations are likely to have on the protein, and thereby predict which mutants will retain biological activity, the skilled artisan would require data regarding, for example, the molecular basis of the protein's activity, its secondary and tertiary structure and the relative importance of any domains of the protein in maintaining said activity, 3) The specification provides no working examples of α- and/or β-globins mutants to show the effects of deletion, substitution and/or insertion mutations, 4) the nature of the invention is a combination of a plant oxygen-binding group with an animal protein, 5) the prior art contains no such teaching except applicants' own art, 6) the level of skill in this art is very high, 7) the predictability of the effect that different substitution, deletion and/or insertion mutations are likely to have on the protein is low, and 8) the breadth of the claims is very large.

Thus, when all the Wands factors are considered together, the conclusion that the practice of the claimed invention would require undue experimentation is inescapable.

4. Claims 43-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 43, 44 and 50-52 are directed to any protein of animal origin that will reversibly bind oxygen when combined with a plant

porphyrin nucleus. The specification, however, only provides a single representative example of such a protein (globin). There is no disclosure of any particular structure to function/activity relationship in the single disclosed example. The specification also fails to describe additional proteins by any identifying structural characteristics or properties other than the fact that they reversibly bind oxygen when combined with a plant porphyrin nucleus, for which no predictability of structure is apparent.

Claims 45-49 are directed to any variant of α- and/or β-globin polypeptide chain that will reversibly bind oxygen when combined with a plant porphyrin nucleus. The specification provides no examples of such variants, only the native α- and/or β-globin. There is no disclosure of any particular structure to function/activity relationship in the single disclosed example. The specification also fails to describe additional variants by any identifying structural characteristics or properties other than the fact that they reversibly bind oxygen when combined with a plant porphyrin nucleus, for which no predictability of structure is apparent. Indeed, the definition of a variant of α- and/or β-globin is such that it encompasses literally any protein, which lacks adequate written description as discussed above for claims 43, 44 and 50-52.

The Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original).

Just as the claims at issue in *UC v. Lilly* defined the invention by the function of the claimed DNA (encoding insulin), the instant claims define the claimed products only by the function they are purported to possess. The court held this sort of functional definition insufficient. "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." *UC v. Lilly*, at *24-*25.

It is clear from the instant specification, exactly as in *Lilly*, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of it.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 52 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The statement of intended utility ("for the treatment of . . .") does not further limit the protein of claim 50 since it does not further specify any characteristic of the protein. Thus, the claim is deemed indefinite.

Claim Rejections - 35 USC § 102

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 43-46, 48, 49, 51 and 52 are again rejected under 35 U.S.C. 102(a) as being clearly anticipated by Dieryck et al.

This rejection was explained in the previous Office action.

Claim Rejections - 35 USC § 103

9. Claims 43, 45 and 47 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Dieryck et al.

This rejection was explained in the previous Office action.

10. Claims 43 and 50 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Dieryck et al. in view of Garlick et al.

This rejection was explained in the previous Office action.

Response to Amendment

11. Examiner appreciates the amendments to the claims to clarify them. The rejections under 35 USC 112, second paragraph are withdrawn in view of those amendments as well as applicants' arguments. The rejections under 35 USC 102 and 103 are, however, maintained.

Applicants argue that since Dieryck et al. was published in December 1995 it is unavailable as a reference in view of the French priority date of PCT/FR96/01123 of July 17, 1995. This is not persuasive. Applicants are entitled only to the International Filing Date of July 17, 1996 and, therefore, Dieryck et al. is indeed available as a reference. Applicants may swear back of a reference under 37 CFR 1.131 but, for non-American applicants who are citizens of a WTO member country that mechanism is available beginning only on January 1, 1996. Thus, applicants do not get the benefit of the French priority date.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (703) 308-4471. The examiner can normally be reached Monday - Friday, 9:00 - 5:30. After January 8, 2004 the examiner's new phone number will be (571) 272-0623.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S. F. Low can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Robert A. Wax
Primary Examiner
Art Unit 1653